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ORIGINAL RESEARCH

The Relationship Between Predominant Negative Symptoms and Self-Stigmatization in Clinically Stable Schizophrenia Patients

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Abstract

Objective: Internalized stigma and negative symptoms have deteriorating effects on prognosis and treatment adherence. Therefore, it is important to recognize the interaction between internalized stigma and negative symptoms in patients with schizophrenia. However, the relationships between negative symptom dimensions and internalized stigma are unclear. In this study, we examined the relationship between self-stigmatization and negative symptoms in a homogeneous subgroup of patients with predominant negative symptoms (PNS). At the same time, the relationships between depression severity and perceived social support and self-stigmatization were evaluated.

Methods: Clinically stable schizophrenia patients who were being followed up in a Community Mental Health Center were included in this cross-sectional study. The Positive and Negative Symptom Scale (PANSS), the Brief Negative Symptom Scale (BNSS), the Calgary Depression Scale for Schizophrenia (CDSS) were applied by the clinician to the patients. In addition, the Internalized Stigma of Mental Illness Inventory (ISMI) and Multidimensional Scale of Perceived Social Support (MSPS), which are self-report scales, were given. Scale scores were compared between PNS and non-PNS (NPNS) groups. Correlations between the ISMI scale scores (perceived discrimination, alienation, stereotype endorsement, social withdrawal, and resistance to stigma) and demographic and clinical variables and other scale scores were evaluated. ANCOVA analysis was used to assess the effect of years of education, employment status, and insight level in intergroup comparisons.

Results: The study included 117 patients [mean age = 43.4 (SD = 11.8); 35 females], with 88.9% experiencing self-stigma. The PNS group (n=58) had lower levels of insight, perceived discrimination, and ISMI total score, but higher negative symptoms and BNSS scores, whereas the NPNS group had higher scores on the positive and general subscales of the PANSS. Correlation analysis revealed negative relationships between alienation and perceived discrimination scores, years of education, and all negative symptom scores. ANCOVA results indicated that, after adjusting for education, employment status, and insight level, the difference in perceived discrimination between PNS and NPNS groups remained significant, while the difference in ISMI total score did not. Insight level was the only significant variable affecting ISMI total score in the model.

Conclusion: Patients with PNS have a unique profile in terms of the relationships between self-stigma and negative symptom dimensions. At the same time, an increase in self-stigma was found as the level of insight increased.

Keywords: Self-Stigma, Predominant Negative Symptoms, Schizophrenia, Insight, Perceived Social Support

INTRODUCTION

Schizophrenia has a heterogeneous clinical presentation represented by positive, negative, disorganized, emotional and cognitive symptoms (1). Especially negative symptoms cause functional impairment due to their resistance to treatment and represent a major unmet therapeutic need in schizophrenia (2). Negative symptoms have high stability in follow-up studies and persist after treatment in 35-70% of patients (3). Therefore, studies to understand the underlying causes of negative symptoms have gained momentum in the last 20 years (2, 4).

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Negative symptoms include deficits in motivation, communication and affect and it is thought that evaluating negative symptoms across different dimensions rather than as a unified structure provides deeper insight into psychopathology (5). It has been shown that the dimensions of negative symptoms also vary in terms of neurobiological correlations (4). According to the most robust model, negative symptoms can be represented by two main factors and five dimensions: reduced expression (alogia and blunted affect) and motivation (asociality, apathy and anhedonia) (3). Studies show that deconstructing the negative symptom structure is valuable in analyzing heterogeneous clinical presentation (4,5).

To overcome the confounding effects of clinical heterogeneity, obtaining homogeneous groups is crucial for a clearer understanding of pathophysiology and the development of effective treatment approaches. In addition to elucidating symptom dimensions, identifying patients with "predominant negative symptoms" (PNS) is considered a valid approach among the strategies proposed to reduce heterogeneity (2,6). PNS refer that negative symptoms are more severe than positive symptoms at any stage of the illness and regardless of duration (4). Additional criteria such as a Positive and Negative Syndrome Scale (PANSS) positive symptom subscale score below 19 and a negative symptom severity above 21 are also used (4, 7). In a large sample study (n=7450), PNS was found in 50% of patients diagnosed with schizophrenia (8). Patients with PNS are considered as a distinct subgroup of schizophrenia with poor prognosis and dysfunction (3).

Negative symptoms may be primary or secondary to conditions such as depression, extrapyramidal symptoms, social deprivation and substance abuse (6). Secondary negative symptoms are associated with a better response to treatment than primary negative symptoms (3). Therefore, it is important to investigate the secondary causes in detail (7). Internalization of stigma is considered to be a secondary cause that plays a role in the development of negative symptoms (9-11).

Stigma is considered as a situation where "labeling, stereotyping, separation, loss of status and discrimination" occur together. Stigmatizing beliefs and attitudes include increased social distance from patients, beliefs that patients are dangerous, underestimation of their social-academic and professional skills, and beliefs that they cannot be good friends or parents (12-14). Stigmatization in mental illness is one of the main factors influencing treatment response, functionality and prognosis (12). Especially individuals with chronic psychiatric diseases such as schizophrenia are exposed to stigmatization (13). Several studies revealed that stigma is associated with impaired quality of life, increased suicide rate, and impaired treatment compliance (14). At the same time, it has been shown that families often choose social isolation and withdrawal to cope with the negative effects of stigmatization in both schizophrenia and bipolar disorder, depriving themselves and the patient from receiving treatment by hiding the ill family member and delaying treatment seeking (15-17).

On the other hand, stigma is not only imposed by society, but also in the form of self-stigma, which results from the internalization process of public prejudices, leading to a decrease in self-esteem and self-efficacy and delaying the search for psychiatric treatment and recovery (18). The process of internalizing stigma related to psychiatric illnesses is thought to have four main dimensions: alienation, stereotype endorsement, perceived discrimination, social withdrawal, and resistance to stigma (12,13). Alienation includes the patient's feelings of not being a member of society because of their illness, feeling inadequate, and feeling ashamed (18). Stereotype endorsement refers to having negative stereotypes about the disease and applying them to oneself (12). Perceived discrimination refers to the perception of discrimination by others (12,13). Resistance to stigma, unlike the other four dimensions of self-stigma, corresponds to the level of beliefs that counteract stigma (12,13,18).

People with schizophrenia are at high risk of experiencing and internalizing stigma. Self-discrimination and social withdrawal may develop based on the acceptance of stereotypes about people with the illness (stereotype endorsement) (16,17). A recent systematic review showed that internalized stigma is consistently associated with lower self-esteem, hopelessness, and impaired social relationships, as well as increased suicide risk, poorer occupational functioning, and avoidant coping (11). Avoidant coping, which may be a consequence of stigma, may also be a cause of internalized stigma by reducing social support (11). There is also evidence of the protective effects of social support on the development and negative effects of self-stigma (19,20). In addition, self-stigma is thought to be a risk factor for depression and negative symptoms (11,14).

Negative symptoms associated with inadequate utilization of social support systems and depression may lead to difficulties in coping with life and feelings of incompetence (14). It is hypothesized that the challenges associated with

the disease may also contribute to the internalization of stereotypes (12-15). On the other hand, the relationship between negative symptoms and self-stigma remains inconclusive. Some studies have suggested that an increase in the severity of negative symptoms is associated with higher self-stigma scores (9-11,21). However, other studies have found no significant relationship (22-24). Furthermore, one study found a negative correlation between negative symptoms and self-stigma (25). The conflicting results may be due to studies that assessed negative symptoms as a single construct. However, stigma may have specific relationships with different dimensions of negative symptoms. On the other hand, to our knowledge, only one study has investigated the relationship between self-stigma and negative symptom dimensions. Rossi et al (2017) found that avolition predicted internalized stigma and depression scores, but depression did not play a role in the relationship between avolition and internalized stigma (21). The study did not report the relationship between the subdimensions of self-stigma and negative symptoms, nor did it examine the effect of confounding factors such as insight and social support, which have been shown to be important in the development of depression in schizophrenia.

The study of homogeneous subgroups is suggested as the main way to overcome the confusion caused by the heterogeneous structure of schizophrenia. This approach is thought to provide clearer and more specific conclusions. There are no studies that have examined the relationships between negative symptoms and self-stigma in homogeneous subgroups of schizophrenia. The main aim of this study is to examine differences in self-stigma between patients with and without PNS. Another aim of the study was to explore the relationships between internalized stigma and negative symptom dimensions. In addition, the relationships between depression, insight, and social support and self-stigma will be investigated. The level of insight and symptom severity may vary according to the stage of the disease. Fluctuations in clinical status over time may be a confounding factor when evaluating relationships with relatively stable variables such as perceived social support and internalized stigma. Therefore, clinically stable patients were included in the study to control for the effect of disease stage on relationships.

METHODS

Participants

This study, conducted from December 2023 to June 2024, included patients registered at the Community Mental Health Center (CMHC) in Manisa who had been followed for at least one year. The minimum sample size required for inclusion in the study was calculated using G-Power 3.1 and was found to be 128 participants with a Cohen's effect size of 0.25 at the 95% confidence level and a power of 0.80 for hypothesis tests comparing the means of two groups. Considering the possibility of data loss, 160 patients with schizophrenia in stable or remission, randomly selected from medical records, were initially contacted by telephone. Patients who were literate, able to complete self-report scales, and able to sign the informed consent form were included in the study. Exclusion criteria included having a psychotic relapse in the previous six months, missing regular outpatient clinic visits every three months, having a degenerative neurological disease, mental retardation, or a medical condition affecting cognitive function. The dose of antipsychotic medications of all patients was stable for the previous six months. An experienced psychiatrist (CC) conducted a detailed clinical interview using the Structured Clinical Interview for DSM-5 (SCID-5-CV) with patients who could be contacted and agreed to participate in the study to confirm the diagnosis of schizophrenia, either during the home visit or in the clinic. Nine patients were excluded due to the exclusion criteria. Data from 11 patients were not included in the analyses because the scales were not completed correctly. Finally, 128 patients who met the inclusion and exclusion criteria were included in the study (see Figure 1). The participants were aged between 18 and 50 years.

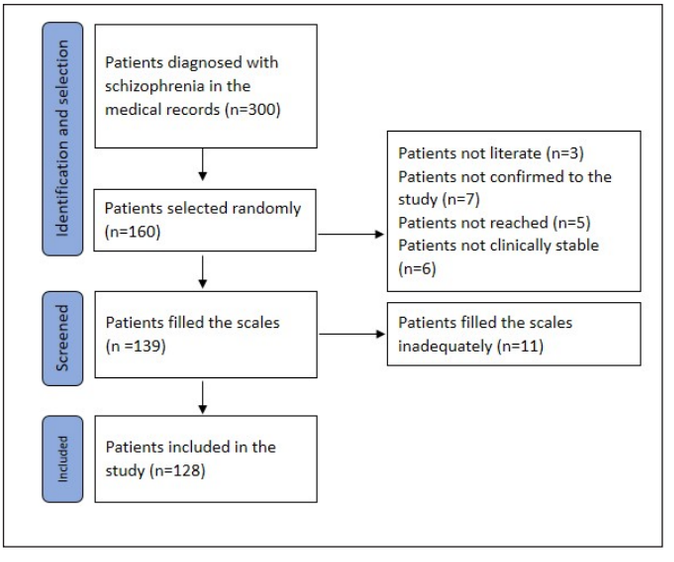

Figure 1. Flow chart of the selection process of the study participants

Ethics committee approval for the study was given by Baskent University Clinical Research Ethics Committee (15/11/2023-23/178). The study was conducted according to the Principles of the Declaration of Helsinki.

CLINICAL ASSESSMENTS

Socio-Demographic and Clinical Data Form

The form includes sociodemographic characteristics as well as information on the medications used by the patient, medication doses, number of hospitalizations and age of onset.

Internalized Stigma of Mental Illness Inventory (ISMI)

The ISMI is 29-item self-report scale that assesses internalized stigma (17,26). The four-point Likert-type scale comprises five subscales: alienation (ISMI-A), stereotype endorsement (ISMI-SE), perceived discrimination (ISMI-PD), social withdrawal (ISMI-SW), and resistance to stigma (ISMI-RS). The items of the ISMI-RS are reverse-scored (15). Higher scores on the ISMI indicate more severe internalized stigma. While calculating the total self-stigma score, the ISMI-RS subscale was excluded in accordance with the literature (27). As widely used in the literature, mean values were calculated for each subscale (subscale score/number of items) and total score (total score/total number of items) (21,28,29). In line with other studies, 2.5 points was taken as the threshold to determine whether self-stigma was present or not (21,28)

Multidimensional Scale of Perceived Social Support (MSPS)

The MSPS is a 12-item, 7-point Likert-type scale of an individual's subjective perception of the adequacy of social support. The scale consists of three subscales: family (MSPS-Fa), friend (MSPS-Fr) and special person (MSPS-SO). It was developed in 1988 by Zimet et al. (30). High scores on the scale indicate a high level of perceived social support. Eker and Arkar conducted the validity and reliability study of the Turkish version of the scale (31).

The Positive and Negative Syndrome Scale (PANSS)

The scale used to assess positive, negative and general psychopathology in patients consists of 30 items on a 7-point Likert scale (1-7). Kostakoğlu et al. conducted the Turkish validity and reliability study of the scale (32). Two negative symptom factors (PANSS-NSF) were also calculated according to specific PANSS items. While emotional withdrawal (N2), passive (N4) and active social withdrawal (G16) were categorized under the experience factor (33), the expression factor includes blunted affect (N1), poor rapport (N3), lack of spontaneity (N6), and motor retardation (G7). The G12 score was used in the assessment of insight.

The Brief Negative Symptom Scale (BNSS)

The BNSS, developed to measure negative symptoms, was adapted to Turkish by Polat et al. (34,35). The scale consists of anhedonia, asociality, avolution, blunted affect and alogia subscales and a total of 13 items. The clinician-administered scale is a 7-point Likert scale (0-6). While anhedonia, asociality and avolition subscale scores indicate the motivation/pleasure factor (BNSS MAP), alogia and blunted affect scores correspond to the emotional expressivity (BNSS EXP) .

The Calgary Depression Scale for Schizophrenia (CDSS)

The semi-structured scale developed to assess depressive symptoms in schizophrenia is a 4-point Likert type (0-3) and consists of 9 items. Aydemir et al. has been conducted the validity and reliability study of the Turkish form of the scale (36).

Criteria of Predominant Negative Symptoms

Operationalized criteria based on expert consensus and existing literature were used for PNS (6,8,37). These criteria included: (i) a baseline score of ≥4 on at least three negative PANSS subscale items or ≥5 on at least two negative PANSS subscale items, (ii) a PANSS positive score under 19, (iii) a PANSS negative subscale score that exceeds the PANSS positive subscale score by a minimum of 6 points, and (iv) a PANSS negative subscale score of at least

Chlorpromazine Equivalent Doses

Chlorpromazine equivalent doses were calculated based on the defined daily doses (DDDs) presented by the World Health Organisation's Collaborative Center for Drug Statistics Methodology (38).

Statistical Analyses

The distribution normality of the variables was evaluated using skewness and kurtosis values. Group comparisons were carried out with independent samples t-tests for continuous variables and chi-squared tests for categorical variables. Effect sizes were determined using Cohen's d formula for the t-test.

Covariance analysis (ANCOVA) was used to statistically control the level of insight, education level and

employment status in between-group comparisons. Pearson correlation coefficient was used for analyzing the relationships between variables. Statistical analyses were performed using SPSS version 23 with a p-value of 0.05 as the significance threshold (SPSS, Chicago, IL, USA).

Continuous variables with a normal distribution are reported as mean ± standard deviation and those without a normal distribution as median (minimum-maximum). Categorical variables are reported as n (%).

RESULTS

Sociodemographic and Clinical Characteristics

The study included 117 patients (age = 43.4 ± 11.8; 35 female) and 104 patients (88.9%) had self-stigma. 58 (49.6%) of the patients were classified as PNS and 59 as non-PNS (NPNS). Marital status, duration of illness, chlorpromazine equivalent dose, and number of hospitalizations were similar between the two groups (PNS vs. NPNS). Age, male sex, unemployment and age of onset were higher in the NPNS, whereas years of education were higher in the PNS group (see Table 1). In addition, there were no significant differences in ISMI scores between males and females. The stigma score of the unemployed patients was significantly higher than employed patients [t(115)= – 3.047; p=0.003]. Descriptive variables for all participants (PNS plus NPNS) and for each group, as well as the results of the comparison between groups are presented in Table 1.

While 15 patients (10 NPNS and 5 PNS) were using a combination of first and second generation antipsychotics, 99 patients (46 NPNS and 53 PNS) were on only second-generation antipsychotics and three patients (3 NPNS) were on only first-generation antipsychotics.

A significant difference was found between groups in clinical scale scores. PANSS positive subcale, level of insight, CDSS total score, perceived discrimination subcale and total scores of ISMI were lower in the PNS group with medium to large effect sizes (Cohen's d = 0.395-0.683) (see Table 1 and 2). Negative, general psychopathology subscales and total scores of PANSS, experiential factor, and expressive factors of the PANSS, all scores of the BNSS, as well as family subscale and total scores of the MSPS were higher in the PNS group with effect sizes of medium to large (Cohen's d = 0.404-3.053).

Correlations Between Internalized Stigma and Clinical Variables

Correlations between internalized stigma and clinical variables were evaluated in all patients. There was no significant correlation between age, duration of illness and daily dose of antipsychotic medication and any ISMI score. The correlation analysis revealed a negative relationship between years of education and scores of the ISMI-A (r = – 0.296; p = 0.001), the ISMI-PD (r = – 0.240; p = 0.009) and ISMI total score (r = – 0.268; p = 0.004).

Negative and general subscales of the PANSS, as well as the negative symptom factors of the PANSS (experiential and expression deficits) and all scores of the BNSS, were negatively correlated with scores of the ISMI-A (rho values between – 0.339 and – 0.221; all p<0.05), the ISMI-PD (rho values between – 0.319 and – 0.208; all p<0.05), and ISMI total score (rho values between – 0.461 and – 0.198; all p<0.05). In addition, higher scores on the ISMI-A, ISMI-PD, and ISMI-SE were associated with better insight. The ISMI-SE score was positively correlated with the positive and general subscales and the total score of the PANSS. No significant relationships were found between social support and depression severity and internalized stigma scores (see supplemental Table S1).

In the analyses performed in the PNS and NPNS groups, there was only one significant correlation in the NPNS group. A positive correlation was found between positive symptom severity and ISMI-SE in the NPNS group (r=0.285; p=0.029). The correlation patterns in the PNS group were the same as those observed in the overall sample, except for one relationship: there was no significant correlation between positive symptoms and the ISMI-SE in the PNS group (r = – 0.143; p = 0.283).

Results of the Analysis of Covariance

There were significant correlations between the ISMI-A score and years of education, total negative symptom score, negative symptom dimensions, and level of insight. In addition, there was a significant difference in the ISMI-A score between employed and unemployed patients. To evaluate the covariate effect of these variables on the difference between the PNS and NPNS groups in terms of ISMI-PD and ISMI total score, an ANCOVA analysis was performed. Due to the high correlation of all negative symptom scores with each other and with the group variable, negative symptom scores were not included in the model to avoid multicollinearity.

After controlling for years of education, employment status, and insight level, the difference between the PNS and NPNS groups on the ISMI-PD remained significant [F(1,112) = 4.418; p = 0.038; ηp^2 = 0.038]. However, the difference in ISMI total score between groups was no longer significant (F(1,112) = 0.523; p = 0.471; ηp^2 = 0.050). Insight level was the only variable with a significant effect in the model (p = 0.001).

Table 1. Demographic and Clinical Characteristics of Patients

	Total Sample (n=117)	PNS (n=58)	Non-PNS (n=59)	Statistics	p
Age	43.40 ± 11.18	40.38 ± 8.42	46.37 ± 12.73	t(115)=2.998 d = 0.556	**0.003****
Female, n(%)	35 (29.90)	25 (43.86)	10 (17.86)	χ2(1)=9.543	**0.002****
Years of education	9.98 ± 4.73	11.55 ± 4.64	8.44 ± 4.32	t(115)=-3.758 d = 0.687	**<0.001*****
Marital status, n(%)					
Married	48 (41.00)	28 (48.30)	20 (33.90)	χ2(1)=2.499	0.110
Unmaried	69 (59.00)	30 (51.70)	39 (66.10)		
Employment, n(%)					
Employed	29 (24.80)	20 (34.50)	9 (15.30)	χ2(1)=5.801	**0.016***
Unemployed	88 (75.20)	38 (65.50)	50 (84.70)		
Age of onset	24.79 ± 8.07	23.14 ± 5.75	26.42 ± 9.61	t(114)=2.249 d = 0.417	**0.027***
Duration of illness	18.62 ± 9.85	17.17 ± 9.08	20.07 ± 10.44	t(114)=1.594 d = 0.296	0.114
CPZ eq. dose (mg/d)	626.81 ± 360.69	645.68 ± 330.81	608.25 ± 389.79	t(115)=-0.560 d = 0.099	0.577
Number of hospitalizations, median(min-max)	2 (0-20)	2 (0-20)	2 (0-20)	U=1403.5	0.093
PANSS Negative	27.16 ± 14.78	39.6 ± 8.07	14.92 ± 8.10	t(115)=-16.510 d = 3.053	**<0.001*****
PANSS Positive	11.64 ± 6.34	9.57 ± 3.11	13.67 ± 7.90	t(115)=3.684 d = 0.683	**<0.001*****
PANSS General	35.82 ± 20.14	41.52 ± 22.77	30.22 ± 15.40	t(115)=-3.149 d = 0.581	**0.002****
PANSS Total	74.61 ± 30.73	90.69 ± 23.72	58.81 ± 28.69	t(115)=-6.546 d = 1.211	**<0.001*****
PANSS NSF-expressive	14.35 ± 6.97	19.91 ± 3.70	8.87 ± 4.73	t(115)=-14.052 d = 2.599	**<0.001*****
PANSS NSF-experiential	10.94 ± 5.70	15.24 ± 3.19	6.72 ± 4.28	t(115)=-12.197 d = 2.257	**<0.001*****
PANSS G12 (Lack of insight)	2.48 ± 1.75	3.03 ± 1.93	1.93 ± 1.36	t(115)=-3.576 d = 0.659	**0.001****
BNSS Anhedonia	14.68 ± 6.54	18.69 ± 4.53	10.73 ± 5.79	t(115)=-8.276 d = 1.531	**<0.001*****
BNSSS Asociality	8.04 ± 3.48	10.26 ± 2.03	5.86 ± 3.22	t(115)=-8.814 d = 1.635	**<0.001*****
BNSS Avolition	7.96 ± 3.55	10.29 ± 1.96	5.66 ± 3.26	t(115)=-9.307 d = 1.721	**<0.001*****
BNSS Alogia	7.35 ± 3.70	9.90 ± 2.01	4.85 ± 3.26	t(115)=-10.073 d = 1.864	**<0.001*****
BNSS Blunted Affect	11.12 ± 5.45	15.03 ± 3.00	7.27 ± 4.50	t(115)=-10.960 d = 2.029	**<0.001*****
BNSS MAP	30.68 ± 12.96	39.24 ± 7.38	22.25 ± 11.69	t(115)=-9.381 d = 1.738	**<0.001*****
BNSS EXP	18.47 ± 9.01	24.93 ± 4.69	12.12 ± 7.60	t(115)=-10.946 d = 2.029	**<0.001*****
BNSS total	49.15 ± 21.57	64.17 ± 11.66	34.37 ± 18.68	t(115)=-10.33 d = 1.913	**<0.001*****
CDSS total	5.45 ± 5.22	4.43 ± 5.00	6.46 ± 5.27	t(115)=2.133 d = 0.395	**0.035***

PNS: Predominant negative symptoms; PANSS: Positive and Negative Syndrome Scale; PANSS NSF-expressive: The expressive factor of the negative symptom factor in the PANSS; PANSS NSF-experiential: The experiential factor of the negative symptom factor in the PANSS; BNSS: Brief Negative Symptom Scale; BNSS MAP Factor: BNSS motivation/pleasure factor; BNSS EXP Factor: BNSS emotional expressivity factor; CDSS: Calgary Depression Scale for Schizophrenia

d :Cohen's d; t: t-test statistic; U: U-statistic; min-max: minimum-maximum

*p<0.05, **p<0.001, ***p<0.001

Table 2. Between Group Comparison of Self-Stigma and Perceived Social Support

	Total Sample (n=117)	PNS (n=58)	Non-PNS (n=59)	Statistics	p
ISMI-A	2.75 ± 0.39	2.68 ± 0.42	2.82 ± 0.36	t(115)=1.886 d = 0.357	0.062
ISMI-SE	2.74 ± 0.31	2.73 ± 0.32	2.74 ± 0.30	t(115)=0.205 d = 0.032	0.838
ISMI-PD	2.81 ± 0.45	2.67 ± 0.47	2.94 ± 0.37	t(115)=3.428 d = 0.638	**0.001****
ISMI-SW	2.78 ± 0.38	2.76 ± 0.38	2.80 ± 0.39	t(115)=0.495 d = 0.103	0.621
ISMI-RS	2.26 ± 0.46	2.29 ± 0.42	2.23 ± 0.50	t(115)=-0.773 d = 0.129	0.441
ISMI Total	2.77 ± 0.20	2.71 ± 0.22	2.82 ± 0.18	t(115)=2.805 d = 0.547	**0.006****
MSPS-SO	11.23 ± 3.20	11.26 ± 3.53	11.20 ± 2.88	t(115)=-0.093 d = 0.019	0.926
MSPS-Fr	11.38 ± 3.01	11.60 ± 2.77	11.17 ± 3.24	t(115)=-0.779 d = 0.143	0.438
MSPS-Fa	11.56 ± 2.84	12.22 ± 2.77	10.92 ± 2.79	t(115)=-2.549 d = 0.467	**0.012***
MSPS Total	34.18 ± 4.53	35.09 ± 4.51	33.29 ± 4.41	t(115)=-2.179 d = 0.404	**0.031***

MSPS-SO: Significant others subcale of Multidimensional Scale of Perceived Social Support; MSPS-Fr: Friends subscale of MSPS; MSPS-Fa: Family subscale of MSPS; ISMI-A: Alienation subscale of Internalized Stigma of Mental Illness Inventory; ISMI-SE: Stereotype endorsement subscale of ISMI; ISMI-PD: Perceived Discrimination subscale of ISMI; ISMI-SW: Social Withdrawal subscale of ISMI; ISMI-RS: Stigma Resistance subscale of ISMI
d :Cohen's d
*p<0.05, **p<0.001, ***p<0.001

DISCUSSION

This study investigated the factors associated with internalized stigma in PNS and NPNS groups. Our findings indicate that perceived discrimination and total internalized stigma are lower in the PNS group. At the same time, all negative symptom dimension scores, insight level and years of education and alienation were negatively correlated with scores of perceived discrimination and total self-stigma. The difference between the groups in terms of total self-stigma was associated with insight level.

To our knowledge, this is the first study to examine self-stigma in patients with PNS. Predominant negative symptoms are known to be associated with poorer prognosis and loss of functioning (37). At the same time, negative symptoms, along with cognitive impairment, are among the symptoms most associated with impaired functioning in schizophrenia. Therefore, it was expected that self-stigma would be higher in patients with PNS than in other patients. On the other hand, contrary to our hypothesis, ISMI-PD and total self-stigma scores were lower in the PNS group. There are mixed findings in the literature regarding the relationship between negative symptoms and self-stigma (9,11,19,21-23,27-29,39-41). Some studies found no relationship between negative symptoms and self-stigma, while others found a positive relationship. A study conducted in China reported a negative association between ISMI-SE, ISMI-PD, and ISMI-SW scores and total negative symptom severity (25). The discrepancies in the literature may be due to factors such as the inclusion of patients at different stages in the studies and the lack of homogeneous groups (29). Our study is the first to investigate the relationship between self-stigmatization and clinical characteristics in homogeneous subgroups of clinically stable patients. Therefore, it may point to more specific results. However, another possible reason

that could explain our findings is a possible confounding effect of exposure to stigma, which was not assessed in our study. Positive symptoms that lead to schizophrenia patients being seen as dangerous have been shown to be more associated with avoidance of others and increased social distance from patients (10,42,43). Therefore, the possible relatively lower stigma experienced by patients with PNS may have led to lower internalized stigma scores. It is recommended that future studies assess self-stigma and perceived stigma together.

Our study also investigated the association between negative symptom dimensions and self-stigma. The only study in the literature so far examining this association found a positive correlation between avolition and total self-stigma, independent of the severity of depressive symptoms (21). According to our findings, there were also negative correlations between the ISMI-A, the ISMI-PD and total self-stigma and total negative symptom severity and all dimensions of negative symptoms (anhedonia, alogia, avolition, asociality, blunted affect). At the same time, in line with the literature, no significant correlations were found between the severity of depressive symptoms and self-stigma and negative symptoms (21). The negative correlations between the ISMI-A and the ISMI-PD and negative symptom severity may be related to lower unmet expectations as a result of lower social motivation. Indeed, in our study negative correlations were observed between asociality and BNSS motivation/pleasure dimensions and scores of the ISMI-A and the ISMI-PD. However, follow-up studies examining negative symptom dimensions are needed to draw clear inferences.

Positive symptoms are thought to increase the risk of exposure to stigmatizing experiences and the likelihood that patients will internalize and accept as true negative beliefs and emotions arising from stigmatizing experiences (44). In our study, in line with the literature, positive symptoms were positively correlated with endorsement of stereotypes (13,45,46). Stereotype endorsement is also associated with insight into the disease, which is thought to play a role in the process of internalization of stigma (47). In our study, the ISMI-SE score was associated with better insight in the NPNS group. In addition, insight was also found to be related to other dimensions of self-stigma. The ISMI-A and the ISMI-PD were related with better insight in the PNS group and all sample, but not in the NPNS group. The associations between insight and self-stigma in the PNS group may be due to the fact that insight leads to a more heightened sense of the impact of social exclusion and isolation secondary to negative symptoms. Consistent with our findings, studies have found that insight is associated with increased internalized stigma (47,48). Internalized stigma was mostly considered as a unitary concept in the relevant studies. However, in a study investigating the relationship between the subdimensions of internalized stigma and insight, more alienation was found in patients with higher levels of insight, supporting our findings (49). Awareness of one's illness and its consequences may lead to alienation, which is characterised by feeling different and lonely because of the illness.

In our study, the level of insight significantly influenced the difference between the PNS and NPNS groups on the total self-stigma score, but not on the ISMI-PD score. In the NPNS group with higher positive symptoms, social sensitization associated with efforts to conceal symptoms or expectations of greater social participation may lead to perceived discrimination independently of insight. This hypothesis needs to be tested in further studies. Consistent with findings in the relevant literature, our study has identified a negative relationship between educational level and self-stigma (50,51). It is believed that highly educated patients have a higher level of knowledge about mental illnesses and possess cognitive resources that enable them to perceive themselves as less differentiated from others (51). On the other hand, no relationship was found between education level and resistance to stigma, which evaluates positive benefits associated with the disease and its consequences. Therefore, it is assumed that higher levels of education allow for a more neutral perspective on the disease process.

In our study, we did not find an association between the severity of depressive symptoms and self-stigma. Self-stigma has been reported to be associated with hopelessness, low self-esteem and depression in several studies (22,24,52). However, in parallel with our findings, a study conducted in Egypt found that the severity of depressive symptoms was independent of self-stigma (53). The study showed that positive coping strategies were protective with regard to depressive symptoms. Another study found that the relationship between self-stigma and depression was moderated by coping mechanisms (52). Therefore, our findings that depressive symptoms are not related to internalized stigma may be due to the possible effects of coping mechanisms that were not accounted for in our study. Some studies have shown that another protective factor for self-stigma is perceived social support (19,20). However, there is also evidence that, similar to our findings, social support has

no effect on self-stigma (54). Perceived social support is a complex process shaped by psychopathology and environmental factors. Therefore, variables such as level of social support, economic and social opportunities, and caregiver characteristics that were not assessed in our study may have influenced our findings. There is limited evidence in the literature on the relationship between social support and self-stigmatization. Large-sample studies examining the relationship between perceived social support and self-stigma in schizophrenia in our country may guide support systems.

Internalized stigma was present in 88.9% of patients. In studies covering the whole of Europe, this rate was found to be 40% (55). Sociocultural differences may explain the different rates. The rate of self-stigma has not been reported in other studies conducted in our country. On the other hand, stigma rates in other studies are similar to our findings (56-58). A study of patients recruited from a CMHC found similarly high rates (57). Multicenter studies comparing patients in different countries are needed to investigate the sociocultural reasons for high stigmatization rates. Identifying regional differences in the dimensions of self-reported stigma may help guide interventions to improve patients' quality of life (29).

LIMITATIONS

The results of this study should be considered in the context of several limitations. First, our relatively small sample size did not allow for further analysis. Larger sample sizes in further studies may allow for structural equation modelling. At the same time, a larger sample size may allow mixed design analyses that draw clearer conclusions by grouping patients by level of stigma in PNS and NPNS groups. Second, self-report scales with potential risk of response bias were used to evaluate self-stigma and perceived social support. On the other hand, there is no structured measurement tools assess these variables. Third, our study is cross-sectional. Follow-up studies can help evaluate the direct effect of self-stigma on negative and depressive symptoms. Fourth, enrolling all patients from a community mental health center limits the generalizability of the results.

Despite these limitations, we believe that our study will make an important contribution to the literature since it is the first study to examine the relationship between negative symptom dimensions and self-stigma dimensions in patients with predominant negative symptoms, controlling for depression level and perceived social support.

CONCLUSION

This study revealed significant relationships between perceived discrimination and alienation and negative symptoms in patients with predominant negative symptoms. In addition, the level of insight was shown to influence the total self-stigma score. The results of the study indicate that negative symptoms should be taken into account when examining self-stigma in schizophrenia and that analyses conducted in homogeneous groups are crucial. At the same time, when compared with the literature, the results suggest that self-stigma may be influenced by socio-cultural or regional factors. Multicenter studies can provide valuable insights into understanding patients' needs and directing preventive interventions.

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Table S1. Correlations Between Internalized Stigma and Clinical Variables

	ISMI-A	ISMI-SE	ISMI-PD	ISMI-SW	ISMI-RS	ISMI total
Age	r= 0.117	r= 0.042	r= 0.099	r= – 0.012	r= – 0.094	r= 0.115
	p= 0.210	p= 0.653	p= 0.289	p= 0.900	p= 0.313	p= 0.218
Years of education	r=-0.296***	r= – 0.051	r= – 0.240**	r= 0.017	r= 0.075	r= – 0.268**
	p= 0.001	p= 0.586	p= 0.009	p= 0.854	p= 0.420	p= 0.004
Duration of illness	r= 0.001	r= – 0.071	r= 0.083	r= 0.007	r= 0.0	r= 0.010
	p= 0.995	p= 0.450	p= 0.373	p= 0.943	p= 0.996	p= 0.915
CPZ eq. dose (mg/d)	r= 0.173	r= – 0.061	r= – 0.027	r= – 0.062	r= – 0.104	r= 0.015
	p= 0.062	p= 0.512	p= 0.777	p= 0.508	p= 0.264	p= 0.870
Number of hospitalization	r= – 0.060	r= – 0.064	r= – 0.024	r= – 0.007	r= 0.088	r= – 0.072
	p= 0.524	p= 0.498	p= 0.795	p= 0.941	p= 0.35	p= 0.443
PANSS Negative	r= – 0.253**	r= – 0.051	r= – 0.319***	r= – 0.017	r= 0.042	r= – 0.298**
	p= 0.005	p= 0.585	p<0.001	p= 0.858	p= 0.653	p= 0.001
PANSS Positive	r= 0.014	r= 0.235*	r= 0.089	r= 0.024	r= 0.027	r= – 0.046
	p= 0.884	p= 0.011	p= 0.337	p= 0.796	p= 0.772	p= 0.622
PANSS General	r= – 0.337***	r= – 0.236*	r= – 0.256**	r= – 0.161	r= 0.085	r= – 0.461***
	p<0.001	p= 0.010	p= 0.005	p= 0.083	p= 0.364	p<0.001
PANSS Total	r= – 0.339***	r= – 0.228*	r= – 0.303***	r= – 0.108	r= 0.081	r= – 0.455***
	p<0.001	p= 0.013	p<0.001	p= 0.244	p= 0.384	p<0.001
PANSS G12 (Lack of insight)	r= – 0.242**	r= – 0.263**	r= – 0.209*	r= – 0.111	r= – 0.036	r= – 0.382***
	p= 0.009	p= 0.004	p= 0.024	p= 0.232	p= 0.702	p<0.001
PANSS NSF-experiential	r= – 0.278**	r= – 0.046	r= – 0.278**	r= – 0.083	r= 0.034	r= – 0.321***
	p= 0.002	p= 0.623	p= 0.002	p= 0.373	p= 0.717	p<0.001
PANSS NSF-experiential	r= – 0.250**	r= – 0.086	r= – 0.304**	r= – 0.034	r= 0.012	r= – 0.314**
	p= 0.006	p= 0.358	p= 0.001	p= 0.715	p= 0.896	p= 0.001
BNSS total	r= – 0.248**	r= – 0.01	r= – 0.268**	r= 0.023	r= 0.002	r= – 0.236*
	p= 0.007	p= 0.916	p= 0.003	p= 0.803	p= 0.987	p= 0.010
BNSS Anhedonia	r= – 0.222*	r= 0.018	r= – 0.300**	r= 0.079	r= 0.016	r= – 0.200*
	p= 0.016	p= 0.845	p= 0.001	p= 0.4	p= 0.867	p= 0.031
BNSS Alogia	r= – 0.222*	r= – 0.057	r= – 0.238**	r= 0.093	r= 0.011	r= – 0.198*
	p= 0.016	p= 0.538	p= 0.010	p= 0.320	p= 0.908	p= 0.032
BNSS Asociality	r= – 0.289**	r= – 0.019	r= – 0.208*	r= – 0.082	r= – 0.046	r= – 0.282**
	p= 0.002	p= 0.837	p= 0.025	p= 0.382	p= 0.624	p= 0.002
BNSS Blunted Affect	r= – 0.237*	r= – 0.012	r= – 0.246**	r= – 0.020	r= 0.005	r= – 0.241**
	p= 0.010	p= 0.899	p= 0.007	p= 0.834	p= 0.954	p= 0.009
BNSS Avolition	r= – 0.221*	r= 0.003	r= – 0.246**	r= 0.01	r= 0.006	r= – 0.213*
	p= 0.016	p= 0.973	p= 0.007	p= 0.915	p= 0.951	p= 0.021
BNSS MAP	r= – 0.250**	r= 0.005	r= – 0.275**	r= 0.021	r= – 0.003	r= – 0.235*
	p= 0.006	p= 0.958	p= 0.003	p= 0.826	p= 0.976	p= 0.011
BNSS EXP	r= – 0.235*	r= – 0.031	r= – 0.247**	r= 0.026	r= 0.008	r= – 0.228*
	p= 0.011	p= 0.742	p= 0.007	p= 0.779	p= 0.934	p= 0.014
CDSS Total	r= – 0.037	r= – 0.161	r= – 0.016	r= – 0.002	r= 0.177	r= – 0.098
	p= 0.689	p= 0.083	p= 0.866	p= 0.983	p= 0.056	p= 0.293
MSPS-SO	r= – 0.040	r= – 0.009	r= – 0.013	r= – 0.114	r= 0.012	r= – 0.084
	p= 0.665	p= 0.922	p= 0.885	p= 0.22	p= 0.901	p= 0.370
MSPS-Fr	r= – 0.055	r= 0.042	r= – 0.136	r= 0.076	r= – 0.025	r= – 0.035
	p= 0.555	p= 0.655	p= 0.143	p= 0.417	p= 0.785	p= 0.711
MSPS-Fa	r= 0.098	r= – 0.102	r= – 0.075	r= – 0.031	r= 0.115	r= – 0.047
	p= 0.292	p= 0.276	p= 0.423	p= 0.739	p= 0.218	p= 0.618
MSPS Total	r= – 0.004	r= – 0.042	r= – 0.147	r= – 0.050	r= 0.063	r= – 0.111
	p= 0.970	p= 0.650	p= 0.114	p= 0.593	p= 0.498	p= 0.233

PANSS: Positive and Negative Syndrome Scale; PANSS NSF-experiential: The experiential factor of the negative symptom factor in the PANSS; PANSS NSF-expressive: The expressive factor of the NSF in the PANSS; BNSS: Brief Negative Symptom Scale; BNSS MAP Factor: BNSS motivation/pleasure factor; BNSS EXP Factor: BNSS emotional expressivity factor; CDSS: Calgary Depression Scale for Schizophrenia; MSPS-SO: Significant Others subcale of Multidimensional Scale of Perceived Social Support; MSPS-Fr: Friends subscale of MSPS; MSPS-Fa: Family subscale of MSPS; ISMI-A: Alienation subscale of Internalized Stigma of Mental Illness Inventory; ISMI-SE: Stereotype endorsement subscale of ISMI; ISMI-PD: Perceived Discrimination subscale of ISMI; ISMI-SW: Social Withdrawal subscale of ISMI; ISMI-RS: Stigma Resistance subscale of ISMI

*p<0.05, **p<0.001, ***p<0.001